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10/737,403

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EXAMINER

WOOLWINE, SAMUEL C

ART UNIT

PAPER NUMBER

1637

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|---------------------------------------|--|
| Office Action Summary | Application No. 10/737,403 | Applicant(s) WILLSON ET AL. | |
| | Examiner SAMUEL WOOLWINE | Art Unit 1637 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 January 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status

Applicant's reply filed 01/22/2008 is acknowledged. Claims 1-24 are pending.

The objection to claim 9 made in the Office action dated 09/19/2007 is withdrawn in view of Applicant's amendment.

The rejection of claims 3-6, 8-10, 12 and 19-22 under 35 U.S.C. 112, 2nd paragraph, made in OA 09/19/2007, are withdrawn in view of Applicant's amendments.

The rejection of claims 1-4, 6-8, 10, 14 and 16 under 35 U.S.C. 102(b) over Verdine et al (WO 98/00435) is withdrawn in view of Applicant's amendment to claim 1. Verdine does not teach exposure of purine bases by a process selected from thermal denaturation/renaturation, alkaline denaturation, or restriction enzyme digestion yielding single-stranded overhangs. Rather, Verdine uses chemical denaturation (i.e. treatment with guanidinium-HCl, a chaotropic agent).

The rejection of claims 1, 2, 5, 7, 8 and 19 under 35 U.S.C. 102(b) over Heisler et al (US Pat 5,843,654) is withdrawn in view of Applicant's amendment to claim 1. Heisler does not teach exposure of purine bases. Rather, Heisler's affinity handle is histidine residues incorporated in a protein.

The rejection of claims 1-4, 7, 9-12, 16 and 20-22 under 35 U.S.C. 102(b) over Pham et al (BioTechniques 20(3):492-497 (1996)) is withdrawn in view of Applicant's amendment to claim 1, which now recites " 'affinity handles' from shielded purine base sites".

The rejection of claims 1-4, 6, 14-17, 23 and 24 under 35 U.S.C. 102(e) over Willson et al (US 2004/0152076) and 35 U.S.C. 102(a) over Murphy et al (WO 02/46398) are maintained as still applicable to the amended claims and as further explained below.

New Rejections

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. There are multiple issues under this section:

With regard to claim 1...

1. The phrase “exposure, enhancement, or stabilization of structural “affinity handles” *from* shielded purine base sites previously present” is vague and indefinite. Does this mean the "affinity handles" consist of or comprise shielded purine base sites? And if the purine base sites are "shielded", are they "affinity handles" in that state? Or must they first be "un-shielded" (e.g. by "exposure")? Furthermore, the examiner was unable to find any use of the term “shielded purine base” in the original disclosure (hence the NEW MATTER rejection below). See below for recommended language. For purposes of examination over the prior art, the examiner will interpret this language to mean that the “affinity handles” comprise purine bases, which were “shielded” (i.e. involved in base pairs with complementary bases) but have been “un-shielded” by

selective thermal denaturation/renaturation, alkaline denaturation, or use of restriction enzymes yielding single-stranded overhangs.

2. In the phrase “selectively to either the desired or undesired moieties or nucleic acid”, the word “selectively” is unnecessary. Furthermore, the word “to” does not make sense in the context of the claim as amended. Previously, the claim recited, as an option, “introduction” of structural affinity handles, and here the word “to” would make sense. However, since the claim now recites only “exposure, enhancement, or stabilization”, the word “to” should become “in” or “within”. One could expose, enhance or stabilize structural affinity handles *within* either the desired or undesired moieties or nucleic acid. See below for recommended language.

Since all other claims depend directly or indirectly from claim 1, they are rejected for the same reasons.

The following language for claim 1 is recommended as a guideline:

A scalable process for the highly selective, high yield separation of a desired product, which may be a nucleic acid or a non-nucleic acid product, from undesired nucleic acid, comprising:

 exposing purine bases present within either the desired nucleic acid product or undesired nucleic acid by a process selected from the group consisting of selective thermal denaturation and renaturation, alkaline denaturation, and restriction enzyme digestion yielding single-stranded overhangs;

 capture of the desired nucleic acid product or undesired nucleic acid by a technique selective for the exposed purine bases;

 and separation of the desired product from the undesired nucleic acid.

Note the above language is not being recommended for the purpose of patentability over the prior art, but merely to overcome the issues under the 35 U.S.C. 112, 2nd paragraph rejection discussed above. Furthermore, should Applicant decide to adopt this suggested language, or otherwise amend claim 1, Applicant should *carefully* review the depending claims to ensure they are consistent with claim 1 to avoid further rejections under 112, 2nd paragraph.

With regard to claims 7 and 10, these claims depend from claim 1 and further recite “introducing” the handles. However, claim 1 has been amended to remove the option of “introducing” the handles, and furthermore requires the handles to comprise purine base sites “previously present”. It is unclear how the handles can be required to be both “introduced” and “previously present”. This creates a paradox which prevents any meaningful interpretation of claims 7 and 10 for examination over the prior art. Therefore, claims 7 and 10 will not be further examined.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

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one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claim 1 has been amended to recite the term "shielded purine base sites". The examiner was unable to find such a term in the disclosure as filed. While there is support for denaturing double-stranded nucleic acid to expose purine bases, and purine bases in a double-stranded nucleic acid could be regarded as "shielded" in this sense, the term "shielded purine base sites" is broader than this particular embodiment. For example, the term "shielded purine base sites" would encompass purine bases modified with a cleavable "caging" or "blocking" group.

Since all other claims depend directly or indirectly from claim 1, they are rejected for the same reasons.

Previous Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 6, 14-17, 23 and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by Willson et al (US 2004/0152076) or alternatively under 35 U.S.C. 102(a) as being anticipated by Murphy et al (WO 02/46398). As the disclosures of these references are identical, reference will only be made to teachings in US 2004/0152076.

With regard to claim 1, Willson teaches exposing structural affinity handles from shielded purine base sites previously present by process of selective thermal denaturation and renaturation, thereby inherently producing “non-shielded” purines, followed by capture of the non-shielded purines by IMAC; see paragraphs [0072] and [0110]. Willson also teaches exposing such affinity handles by producing alkaline cell lysates, thus inherently producing alkaline denatured nucleic acid, followed by capture of such denatured nucleic acid on IMAC columns (see paragraphs [0187]-[0190]).

With regard to claims 2 and 4, Willson introduces single-strandedness into the molecules to be captured by either thermal or alkaline denaturation, as discussed for claim 1.

With regard to claim 3, in the example taught by Willson for clarifying a plasmid lysate (paragraphs [0187]-[0190]), a plasmid preparation is sensitive to host genomic DNA contamination.

With regard to claim 6, Willson teaches IMAC (paragraph [0120]).

With regard to claim 14, Willson teaches IMAC (paragraph [0120]), which comprises adsorption on chelated metal (paragraph [0007]).

With regard to claims 15, 16, 17, Willson teaches multi-channel plates ("well plate"), spin columns and magnetic particles (page 5, Table A, Parameter: Support Shape).

With regard to claim 23, Willson teaches HIC (hydrophobic interaction chromatography; page 5, Table A, last 3 lines under heading "Preferred").

With regard to claim 24, Willson teaches RPC (reverse phase chromatography; "Reverse Phase Resin", which implicitly teaches reverse phase chromatography; page 6, Table A, line 2 under heading "Preferred").

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over either Willson et al (US 2004/0152076) or Murphy et al (WO 02/46398) in view of Hawkins (US 5,898,071).

The teachings of Wilson and Murphy have been discussed. Neither of these references teaches processing multiple samples in parallel.

Hawkins teaches methods of nucleic acid purification and teaches that an “advantage of using a microtiter plate is that many samples can be isolated in parallel” (column 10, lines 54-60).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention of the instant application was made to modify the method of either Willson or Murphy to process multiple samples in parallel, because Hawkins teaches this to be advantageous.

Response to Arguments

Applicant's arguments filed 01/22/2008 have been fully considered but they are not persuasive.

With regard to the rejection under 35 U.S.C. 102(a) and (e), Applicant argues that the embodiment cited by the examiner, where a deoxyribose tail is introduced as an affinity handle, does not apply to the amended claims. That is, the introduction of such a tag does not involve exposure, enhancement or stabilization of an affinity handle comprising previously present purine bases by a process of selective thermal denaturation and renaturation, alkaline denaturation or the use of restriction enzymes (pages 12-13 of the response).

This argument is not persuasive, as Willson teaches other embodiments, as discussed in the rejection, which meet the limitations of the amended claims.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAMUEL WOOLWINE whose telephone number is (571)272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SCW

/GARY BENZION/

Supervisory Patent Examiner, Art Unit 1637